DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 March 2008 has been entered.

Response to Remarks

2. Applicant's arguments have been fully considered but they are not persuasive. First, Applicant argues that the combination of Marcelpoil (7,056,236) and Kotera (4,090,243) is invalid because "Kotera does not disclose employing a 'plurality of control samples comprising a single color of interest'" (Remarks, p. 11). That is, Kotera utilizes "n" different control colors and does not create a plurality of control samples for any single color.

While it may be true that Kotera does not utilize more than one control sample per color, the claim does not require this limitation. The claim recites "a plurality of control samples *comprising* a single color of interest." The term *comprising* has been judicially interpreted as referring to an open-ended amount, as opposed to the term *consisting of*, which is close-ended. Therefore, use of the term *comprising* in claim 1 does not limit the number of colors of interest—it only requires that there be at least a single color of interest (i.e., at least one color) for the plurality of control samples. The claim does not preclude there being more than one color of interest for the plurality of control samples.

Furthermore, even if the claim were amended to denote that the plurality of control samples *consists of* only one color of interest, the claim then would appear to contradict the teachings of the Specification at pages 13-14:

The Specification teaches:

> "Using 3 control samples (e.g., slides) each comprising a color (e.g., a stain) with one of the colors (stains) to be measured (called K, lambda, and C) and an experimental sample (e.g., a slide) comprising all 3 colors (e.g., all the stains) on which a sample to be measured is contained, the concentration of each color (e.g., stain) at each pixel can be measured . . ." (p. 13).

This passage establishes that each of the three control samples comprises "a color." The three control samples do not appear to be limited to the same color here. In other words, each of the three control slides contains a color; an experimental slide contains all three of those colors. There is no mention here whether those colors can or must be different or the same.

Next, for each control, a vector of the average RGB values of all pixels are defined (p. 13) and formed into a matrix Q (p. 14). If Q is invertible, then "the 3 colors (e.g., stains) are <u>genuinely different colors (as opposed to shades of the same color)</u>" (p. 14). The inverse of this matrix (Q^{-1}) is then used to transform an experimental sample into a new color space (p. 14). See also pp. 54-55 and figure 10, which discuss generating the inverse of the control matrix for color conversion purposes.

Accordingly, it appears as though the invention requires Q to be invertible so that a color space transformation can be carried out. The Specification teaches that when Q is invertible, the three control colors are "genuinely different colors (as opposed to shades of the same color)."

Therefore, for the invention to be operable, it appears as though the colors of each of the control samples *must* all be different colors. The claims have been construed to correspond to this interpretation.

3. Next, Applicant argues that the combination is invalid because there is no motivation or suggestion to combine the reference teachings (p. 11). Recently, the Supreme Court in *KSR v. Teleflex,* 127 S.Ct. 1727 (2007), repudiated the stringent requirements of the teaching-suggestion-motivation (TSM) test and established that motivation or suggestion does not necessarily need to be present for a claim to be rendered obvious. A claim can be obviated when the prior art teaches a known technique or process that, when applied to a known method, yields predictable results. *Id.* at 1739. Kotera is only relied upon only for the narrow teaching that it was conventional to utilize a plurality of control color samples in a process for identifying the color of experimental samples and that it was also conventional to utilize the average color of each of the control samples as the representative color of each sample. These known methodologies, if applied to Marcelpoil's method, would yield substantially predictable results as explained below.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-17 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 7,065,236 by Marcelpoil et al. ("Marcelpoil") in view of U.S. Patent 4,090,243 by Kotera et al. ("Kotera").

Regarding claims 1 and 10, Marcelpoil discloses a method/program for quantifying color in a sample comprising multiple colors, the method comprising:

measuring a color channel value in a plurality of pixels from a control sample comprising a single color of interest (column 8/14-23: camera 300 captures a color image of a sample 500 – the image having red, green, and blue color channel values);

defining a vector for the control sample, wherein the vector comprises a color channel value present in the control (e.g. the optical density vector OD, given by equations 3-5 or 6-8 in column 11, defines a vector comprising the measured optical densities for the red, green, and blue color channels);

defining a matrix comprising each of the values of each of the color channels (i.e. the matrix formed by the equations associated with the OD vector is defined by equations 21 and 22 in column 14, in order to determine the dye concentrations C based on the known optical densities OD and absorption coefficients ε – see column 14/1-6);

defining a conversion matrix comprising the inverse of the matrix based upon the control measurements (i.e. the conversion matrix denoted by equation 23 in column 14 is defined based upon the measured control optical densities);

measuring color channel values in an image of an experimental sample comprising a plurality of colors of interest, each of the pixels comprising a plurality of color channels (column

16/9-14: an experimental sample having the same dyes uses in the calibration process for determining the conversion matrix is imaged in the same manner as the control sample); and

calculating the amount of a color in the experimental sample by converting the channel values in the experimental sample using the conversion matrix (column 16/14-31: the amount of color, or concentrations of the dyes, in the experimental sample is determined using the conversion matrix).

However, Marcelpoil seems to only utilize a single control sample and does not appear to disclose or suggest using a "plurality of control samples," as claimed. Accordingly, Marcelpoil does not disclose defining the vector or the matrix on the basis of an "average" of color channel values for a "plurality of control samples."

Kotera discloses a system (figures 1A and 1B) for characterizing the colors of a color sample that is very similar to that of Marcelpoil and involves the same concepts of deriving an inverse matrix of mean color intensity values (column 5/1-35) and using the inverse matrix to ascertain the colors of an experimental sample (column 5/58-66). In particular, Kotera teaches that control color prints C1 … Cn, as shown in figure 2, are imaged, and the measured colors and used to determine the conversion matrix. Kotera teaches that each of these control color prints contain a plurality of "elemental areas," which essentially correspond to sub-areas within the larger print area, and the elemental areas are each "microscopically" imaged to generate representative intensity signals thereof (column 1/59 through column 2/3). The mean intensity value μ of each spectral (i.e. color) component for each control color print corresponds to the representative intensity signal of a per-unit area (column 2/18-27). The set of mean values μ, in

conjunction with the set of representative intensity signals, is utilized to obtain the conversion matrix that is used to ascertain the color C_i of a given experimental sample, expressed as the probability $P(C_i)$ that the ascertained color corresponds to the i-th control print (see column 2/22-39 and column 3/57 et seq.).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Marcelpoil by Kotera to achieve the claimed invention by measuring a plurality of control samples and defining the vector and the matrix on the basis of an average of each color channel present in the control samples, since Kotera shows that, for the purposes of identifying experimental color samples based on the known properties of control color samples, it was conventional to microscopically scan multiple control color prints on the basis of a plurality of "elemental" sample areas within the prints and utilize the average of those sample areas as a basis for deriving a conversion matrix, as explained above. Such a modification would achieve substantially the same results as achieved by Marcelpoil since Marcelpoil's control samples are analyzed in a region where two or three dyes are mixed to produce an area of uniform color. In this instance, averaging over the entirety of a color sample would provide a measure of the color of the overall area of the sample instead of one small region within the sample. In addition, utilizing multiple control samples instead of only one would provide more control data with which to process and identify unknown experimental color samples.

Regarding claims 2 and 11, Marcelpoil discloses the color channels comprise red, green, and blue (see figure 1).

Regarding claims 3 and 12, the combination of Marcelpoil and Kotera discloses each control is stained with a single staining reagent to generate a color of interest (column 9/13-17 and column 10/63 et seq. of Marcelpoil: the control is stained with a plurality of staining reagents, including a single marker dye that is used to generate a color of interest).

Regarding claims 4 and 13, Marcelpoil discloses that the experimental sample is stained with a plurality of stains to generate a plurality of colors of interest (column 10/63 et seq.: the sample is stained with e.g. a marker dye and a counterstain).

Regarding claims 5 and 14, Marcelpoil discloses that the number of stains in a experimental sample are less than or equal to the number of color channels (column 16/14-31: concentrations of 3 dyes are determined – with there being 3 color channels).

Regarding claims 6 and 15, Marcelpoil suggests that an image of the experimental sample can be displayed as a monochrome image (see e.g. equation 24, column 16, which quantifies the black and white pixel intensities for the experimental sample image).

Regarding claims 7 and 16, Marcelpoil does not expressly disclose setting all but one of the color channel values to zero in order to determine the amount of a single color in the experimental sample, as claimed, however, such a limitation would have been exceedingly well-known and obvious to those skilled in the art in view of the fact that each of the color channels for an RGB image independently quantify the amount of a single color – red, green, or blue – present in an image, and e.g. the values of red and green channels have no bearing on how much "blue" is exhibited by an image of the sample.

Regarding claims 8 and 17, Marcelpoil discloses rendering a digital display of the experimental sample (i.e. displayed on the computer screen, as shown in figures 1 and 2).

Regarding claim 9, the combination of Marcelpoil and Kotera teaches the computer implemented method of claim 1 (i.e. both Marcelpoil's and Kotera's methods are implemented via a computer).

Regarding claim 22, Marcelpoil discloses that the computer-implemented method can be automated (see column 20/2-14).

6. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 7,065,236 by Marcelpoil et al. ("Marcelpoil") in view of U.S. Patent 4,090,243 by Kotera et al. ("Kotera") and U.S. Patent Application Publication 2004/0114227 by Henderson et al. ("Henderson").

Regarding claim 18, Marcelpoil discloses a machine vision system (figures 1 and 2) for automated analysis of a biological sample on a slide comprising:

a system processor (i.e. computer 350 includes a processor);

a computer program on computer readable medium (column 20/2-14), the computer program comprising an image algorithm comprising instructions to cause the computer to:

measure a color channel value in a plurality of pixels from a control sample comprising a single color of interest (column 8/14-23: camera 300 captures a color image of a sample 500 – the image having red, green, and blue color channel values);

define a vector for the control sample, wherein the vector comprises a color channel value present in the control (e.g. the optical density vector OD, given by equations 3-5 or 6-8 in column 11, defines a vector comprising the measured optical densities for the red, green, and blue color channels);

define a matrix comprising each of the values of each of the color channels (i.e. the matrix formed by the equations associated with the OD vector is defined by equations 21 and 22 in column 14, in order to determine the dye concentrations C based on the known optical densities OD and absorption coefficients ε – see column 14/1-6);

define a conversion matrix comprising the inverse of the matrix based upon the control measurements (i.e. the conversion matrix denoted by equation 23 in column 14 is defined based upon the measured control optical densities);

measure color channel values in an image of an experimental sample comprising a plurality of colors of interest, each of the pixels comprising a plurality of color channels (column 16/9-14: an experimental sample having the same dyes uses in the calibration process for determining the conversion matrix is imaged in the same manner as the control sample); and

calculate the amount of a color in the experimental sample by converting the channel values in the experimental sample using the conversion matrix (column 16/14-31: the amount of color, or concentrations of the dyes, in the experimental sample is determined using the conversion matrix); and

output the amount of color in the experimental sample (column 17/1-19);

a monitor in operable communication with the computer (as shown in figure 1);

an input device in connection with the computer (e.g. keyboard or mouse shown in figure 2);

an optical imaging system (video microscopy system 100) in operable communication with the computer, comprising:

a movable stage (column 18/59-63);

an identification member (column 17/28-45: identification marks produced by an operator);

an optical sensing member (camera 300) in optical communication with the stage configured to acquire an image at a location on a slide and in electrical communication with the processor;

a storage member for storing the location of a candidate object or area of interest (column 17/20-64 and column 19/28-46: the memory of the computer 350 is used to store images containing markings that indicate the locations of areas of interest); and

a storage device for storing each image (column 19/22-32).

However, Marcelpoil seems to only utilize a single control sample and does not appear to disclose or suggest using a "plurality of control samples," as claimed. Accordingly, Marcelpoil does not disclose defining the vector or the matrix on the basis of an "average" of color channel values for a "plurality of control samples."

Kotera discloses a system (figures 1A and 1B) for characterizing the colors of a color sample that is very similar to that of Marcelpoil and involves the same concepts of deriving an inverse matrix of mean color intensity values (column 5/1-35) and using the inverse matrix to ascertain the colors of an experimental sample (column 5/58-66). In particular, Kotera teaches that control color prints C1 … Cn, as shown in figure 2, are imaged, and the measured colors and used to determine the conversion matrix. Kotera teaches that each of these control color prints contain a plurality of "elemental areas," which essentially correspond to sub-areas within the larger print area, and the elemental areas are each "microscopically" imaged to generate

representative intensity signals thereof (column 1/59 through column 2/3). The mean intensity value μ of each spectral (i.e. color) component for each control color print corresponds to the representative intensity signal of a per-unit area (column 2/18-27). The set of mean values μ, in conjunction with the set of representative intensity signals, is utilized to obtain the conversion matrix that is used to ascertain the color C_i of a given experimental sample, expressed as the probability $P(C_i)$ that the ascertained color corresponds to the i-th control print (see column 2/22-39 and column 3/57 et seq.).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Marcelpoil by Kotera to measure a plurality of control samples and define the vector and the matrix on the basis of an average of each color channel present in the control samples, as claimed, since Kotera shows that it was conventional to microscopically scan a control color print on the basis of a plurality of "elemental" sample areas and utilize the average of those sample areas as a basis for deriving a conversion matrix, as explained above. Such a modification would achieve substantially the same results as achieved by Marcelpoil since Marcelpoil's control samples are analyzed in a region where two or three dyes are mixed to produce an area of uniform color. In this instance, averaging over the entirety of a color sample would provide a measure of the color of the overall area of the sample instead of one small region within the sample. In addition, utilizing multiple control samples instead of only one would provide more control data with which to process and identify unknown experimental color samples.

In addition, Marcelpoil discloses that the microscope may include one or more robotic components (column 18/59-63) but does not appear to disclose an automated loading and unloading member for loading and unloading of a slide, as claimed.

Henderson discloses an automated slide loader for use with a microscope. In particular, Henderson teaches that it is advantageous to provide an apparatus that automatically loads and unloads slides to and from a microscope. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Marcelpoil and Kotera to achieve the claimed invention by including an automatic slide loader/unloader, as claimed, since automating a manual procedure has been judicially recognized as per se obvious. See *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Colin M. LaRose whose telephone number is (571) 272-7423. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Werner, can be reached on (571) 272-7401. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000. Any inquiry of a general nature or relating to the status of this application or proceeding can also be directed to the TC 2600 Customer Service Office whose telephone number is (571) 272-2600.

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